

## **REMARKS**

### **I. Substance of the Interview Statement**

Applicants thank Examiner Tran for her time and consideration of the above-identified application in the July 7, 2010, telephone interview with Applicants' representative. As highlighted in the Examiner's Interview Summary dated July 9, 2010, the participants discussed the outstanding rejection under 35 U.S.C. § 112, second paragraph, and amendments to the claims that should be sufficient to overcome the rejection. The claims have been amended accordingly.

### **II. Claim Amendments**

By the foregoing amendments to the claims, claim 63 has been amended to clarify that the particle coatings are "in direct contact" with the surface of the pellets. The amendment is supported throughout the application as filed. In particular, for at least the reasons set forth at pages 9-10 of the response filed on November 12, 2009, a person of ordinary skill in the art would have known that the coating material of the present invention was applied directly onto the surface of the pellets and that the coating material was in direct contact with the surface of the pellets.

This amendment is merely editorial in nature and is not intended to change the scope of the claims or any elements recited therein. The amendments to the claims have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the claims is respectfully requested.

### **III. Response to Election of Species Requirements**

At pages 2-4 of the Office Action, the Examiner has required a further election of species for prosecution on the merits.

In response, Applicants hereby elect 1a), the polymethacrylate material is a methacrylic acid copolymer; 2a), the pH dissolution dependent coating material of the plurality of first particles and second particles are the same; and 3a), the active compounds in the plurality of first

and second particles are the same. The elections are made without prejudice or disclaimer to any non-elected subject matter.

### **III. Response to Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 63-92 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

Not to acquiesce to the rejection, but to advance prosecution in the application, the claims have been amended to recite that the coating of the particles is “in direct contact with” rather than “contiguous with” the surface of the pellets.

Applicants submit that the claims as amended particularly point out and distinctly claim the subject matter Applicants regard as the invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

### **IV. Response to Claim Rejections Under 35 U.S.C. § 102**

*A.* Claims 63-75 and 79 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Fischer et al. (U.S. Patent No. 6,267,990).

*B.* Claims 63-82 and 85 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Heinicke et al. (U.S. Patent No. 5,834,024).

These rejections are respectfully traversed.

As noted above, the claims have been amended to clarify that the coating of the particles is in direct contact with the surface of the pellets. This feature, among others, is not taught or even suggested by Fischer et al. or Heinicke et al.

In particular, Fischer et al. discloses using an undercoat (OPADRY II) between the surface of the pellets and the outer functional coating. Briefly, the purpose of the undercoat is to seal the pellets to moisture and to smooth out the surface of the pellets so that the outer functional coating can be applied at uniform thickness as is conventional in the art of coating with pH-sensitive film forming polymers. However, in contrast to the present claims, Fischer et al. does not disclose an outer functional coating (i.e. a coating “comprising a pH dissolution dependent coating material”) in direct contact with the surface of the pellets. (See pages 11-14 of the November 12, 2009, response for more detail).

Similarly, Heinicke et al. does not teach or even suggest a coating comprising a pH dissolution dependent coating material in direct contact with the surface of the pellets. This has been acknowledged by the Examiner at the paragraph spanning pages 10 and 11 of the Office Action ("there is no disclosure in HEINICKE of coating the surface of a plurality of first and second pellets directly with a pH sensitive material as a film forming material for pH-mediated release of an active agent..."). (See pages 14-15 of the November 12, 2009, response for more detail).

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 102.

#### **V. Response to Claim Rejections Under 35 U.S.C. § 103**

**A.** Claims 63-82 and 85 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Heinicke et al. in view of Fischer et al.

**B.** Claims 63-92 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Speirs (U.S. Patent No. 5,834,021), in view of Andre et al. (EP 1064938 A1).

These rejections are respectfully traversed.

As noted above, neither Heinicke et al. nor Fischer et al. teach or suggest a coating comprising a pH dissolution dependent coating material in direct contact with the surface of the pellets. Similarly, neither Speirs nor Andre et al. teach or suggest a coating comprising a pH dissolution dependent coating material in direct contact with the surface of the pellets. For at least these reasons, the present claims are not obvious over the cited combinations of references.

In particular, pellets formed by extrusion/spheronisation processes inevitably have irregular surfaces. Before the present invention, if the pellets were to be coated with a pH sensitive delayed release coating material, it was routine to provide the pellets with an undercoat to smooth out the surface of the pellets so that a uniform thickness of the pH sensitive functional coating could be applied (see, e.g., Fischer et al.). In this way, once the pH of the surrounding medium reached the pH threshold of the coating, the entire coating would dissolve and/or disintegrate quickly to initiate release of the active agent.

The present inventors have observed for the first time that if the pH sensitive coating is applied directly to the surface of the irregular surface of the pellets, then the release profile is modified. In this connection, instead of the entire coating dissolving quickly, the regions of

thinner coating dissolve before the regions of thicker coating. In this way, initial release may be phased and sustained before the pellets breaks down to provide the bulk of the release.

In addition, as demonstrated by the present Examples, the rate of release of the active unexpectedly increases as the pH increases. This is unexpected as usually pH sensitive coatings remain intact until the pH of the surrounding medium reaches the pH threshold of the coating and the coating degrades quickly at a single site in the intestine. In contrast, the rate of release of active from the pellets of the present invention actually increases as the pellets continue to travel down the intestine and the pH of the intestinal medium increases. In addition, since the pH of the intestines increases from the center of the intestinal lumen to the walls, the rate of release of the active actually increases as the pellets travel nearer to the walls of the intestine, i.e. where release is needed most. Such release does not occur if there is an undercoating to provide uniform thickness of the outcoating.


The references cited by the Examiner, taken alone or in combination, do not teach or suggest coating different pluralities of pellets directly with the recited coating material, nor provide any suggestion that doing so could result in such a favorable release profile. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 103.

**CONCLUSION**

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions related to this response, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney at the below-listed telephone number concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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